Attorney Docket: NEX87/PCT-US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT:	PAGRATIS ET AL	
SERIAL NO.:	10/030,787	EXAMINER: FORMAN, B.J.
FILED:	JANUARY 31, 2002	ART UNIT: 1634
TITLE:	HIGH AFFINITY TGFß NUCLEIC ACID LIGANDS AND INHIBITORS	CONFIRMATION NO. 6400

Mail Stop Appeal Brief
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPEAL BRIEF

Sir:

In regard to the referenced application, Appellant submits this Appeal Brief.

I. REAL PARTY IN INTEREST

The real party in interest is Gilead Sciences, Inc. The right of Gilead Sciences, Inc. to take action in the subject application was established by virtue of the following chain of title:

1. An assignment from the inventors to Gilead Sciences, Inc. is recorded at Reel 012780, Frame 0982.

II. RELATED APPEALS AND INTERFERENCES

The undersigned legal representative of Appellant hereby confirms that there are no known appeals or interferences relating to the present application, or any parent application, which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

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37 CFR 1.8
CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Appeal Brief, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on MAY 31, 2005.

Signature: Tracy E. Crispino
Name: Tracy E. Crispino

III. STATUS OF THE CLAIMS

Claims 2-7 are pending in the application. No claims have been allowed. Claim 1 and claims 8-21 have been cancelled. Claims 2-7 stand rejected under a final Office Action mailed December 7, 2004.

In response to the Final Office Action of December 7, 2004, a signed declaration by co-inventor Pagratis in accordance with 37 C.F.R. § 1.132 in respect of U.S. Pat. No. 6,124,449 (a signed declaration by co-inventor Gold in accordance with 37 C.F.R. § 1.132 in respect of U.S. Pat. No. 6,124,449 was previously submitted on November 24, 2004) and terminal disclaimers in respect of U.S. Pat. Nos. 6,713,616 and 6,346,611 were submitted under 37 C.F.R. § 1.116 on January 31, 2005. The postcard receipt (which was stamped by OIPE) indicates that two terminal disclaimers were submitted; however, it appears that the terminal disclaimer in respect of U.S. Pat. No. 6,713,616 was not received by the Examiner. In a telephone conversation with attorney Steven Hird on February 28, 2005, the Examiner recommended that the Applicants resubmit the terminal disclaimer in respect of U.S. Pat. No. 6,713,616. A copy of the terminal disclaimer filed January 31, 2005 in respect of U.S. Pat. No. 6,713,616 was therefore resubmitted under 37 C.F.R. § 1.116 on February 28, 2005. In view of the declarations and the terminal disclaimers, it is believed that the only issue remaining for appeal is the 35 U.S.C. § 112, first paragraph, rejection of claims 2-7.

IV. STATUS OF THE AMENDMENTS

No amendments to the claims were filed in response to the Final Office Action dated December 7, 2004.

V. SUMMARY OF CLAIMED SUBJECT MATTER

Claim 2 is directed to a complex comprised of a TGFβ2 nucleic acid ligand and a non-immunogenic, high molecular weight compound or lipophilic compound. Support for this claim can be found on page 12, line 30 - page 13, line 1 of the Specification, which provides that in certain embodiments the invention is drawn to "a complex comprising one or more nucleic acid

ligands to TGFβ2 covalently linked with a non-immunogenic, high molecular weight compound or lipophilic compound." Nucleic acid ligands to TGFβ2 are provided in Tables 5, 7, 8, 11, 13, 14, 16-19 and Figure 9. (Specification, pages 60-61, 63-64, 68-70, 72-73, 75-79).

Claims 3 and 4 further define the invention of claim 2. Claim 3 is directed to the complex of claim 2 further comprising a Linker between said ligand and said non-immunogenic, high molecular weight compound or lipophilic compound. (Specification page 14, lines 3-9). Claim 4 is directed to the complex of claim 2 wherein said non-immunogenic, high molecular weight compound is a polyalkylene glycol. (Specification, page 13, lines 8-9).

Claim 5 further defines claim 4. Claim 5 is directed to the complex of claim 4 wherein said polyalkylene glycol is polyethylene glycol (PEG). (Specification, page 13, line 10).

Claim 6 further defines claim 5. Claim 6 is directed to complex of claim 5 wherein said PEG has a molecular weight of about between 10-80 K. (Specification, page 13, line 11).

Claim 7 further defines claim 6. Claim 7 is directed to the complex of claim 6 wherein said PEG has a molecular weight of about 20-45 K. (Specification, page 13, line 12).

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Claims 2-7 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

VII. ARGUMENT

A. The Rejection of Claims 2-7 under 35 U.S.C. § 112, first paragraph

1. Statement of the Relevant Law Pertaining to 35 U.S.C. § 112, first paragraph rejections.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*,

935 F.2d at 1563, 19 USPQ2d at 1116. For original claims, there is a strong presumption that an adequate written description of the claimed invention is present when the application is filed. *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976).

An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406; *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).

A number of factors must be weighed in view of the level of skill and the knowledge in the art in light of the written description. Patents and printed publications in the art should be relied upon to determine whether an art is mature and what the level of knowledge and skill is in the art. *See, Guidelines for Examination of Patent Applications under the 35 USC § 112, para 1, "Written Description" Requirement*, MPEP § 2163 (hereinafter, "*Written Description Guidelines*"). Generally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement. Information which is well known in the art need not be described in detail in the specification. See, e.g., *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986). With regard to mature technologies, the *Written Description Guidelines* state at MPEP § 2163 II.A.3(a) (emphasis added):

> In most technologies which are mature, and wherein the knowledge and level of skill in the art is high, a written description question should not be raised for original claims <u>even if the specification discloses only a method of making the invention and function of the invention</u> See, e.g., *In re Hayes Microcomputer Products, Inc. Patent Litigation*, 982 F.2d 1527, 1534-35, 25 USPQ2d 1241, 1246 (Fed. Cir. 1992).

For each claim drawn to a genus, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A "representative number of species" means that the species which are adequately described are representative of the entire genus. What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. *See Written Description Guidelines*, MPEP § 2163 II.A.3(a) ii). Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. Indeed, there are situations where one species adequately supports a genus. *See, e.g., In re Rasmussen*, 650 F.2d 1212, 1215, 211 U.S.P.Q. 323, 326-27 (C.C.P.A. 1981) (quoting *In re Smythe*, 480 F.2d 1376, 1384, 178 U.S.P.Q. 279, 285 (C.C.P.A. 1973)); *In re Herschler*, 591 F.2d 693, 700, 200 U.S.P.Q. 711, 714 (C.C.P.A. 1981). On the other hand, "a patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when ... the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed." *In re Curtis*, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004).

2. The Rejection of Claims 2-7 under 35 U.S.C. § 112, first paragraph is improper.

Claims 2-7 have been rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed has possession of the claimed invention. The rejection asserts that the claims are drawn to a genus of complexes not described or contemplated, but that specification exemplifies only a single ligand (NX22323) covalently linked to PEG (Example 5). The rejection further asserts that the specification does not teach that the invention is complete as evidenced by the drawings. The rejection also asserts that while the specification teaches methods for isolating target-specific nucleic acid ligands (Examples 2-3) and that high affinity ligands are obtained (page 11), the specification does not

describe identifying characteristics of the claimed complexes which show that the applicant was in possession of the claimed invention.

The level of skill and knowledge in the relevant art, as reflected by patents and printed publications, indicate that the art is mature. This is evidenced by the fact that at the time the application was filed, there were over 70 issued patents in the United States alone with the phrase "nucleic acid ligand" or "SELEX" in their abstracts (using the USPTO's Full-Text database). Furthermore, at the time the application was filed there were numerous publications describing complexes of nucleic acid ligands and various non-immunogenic, high molecular weight or lipophilic compounds. For example, WO 96/34876, published November 7, 1996 describes in detail numerous complexes of nucleic acid ligands and non-immunogenic, high molecular weight or lipophilic compounds, including complexes of nucleic acid ligands to thrombin, basic Fibroblast Growth Factor (bFGF), L-Selectin, and Vascular Endothelial Growth Factor (VEGF). WO 98/18480, published May 17, 1998, discloses in detail complexes of nucleic acid ligands to VEGF and non-immunogenic, high molecular weight or lipophilic compounds. WO 99/3119, published June 24, 1999, discloses in detail complexes of nucleic acid ligands to Platelet Derived Growth Factor (PDGF) and non-immunogenic high molecular weight or lipophilic compounds. U.S. Pat. No. 5,859,228, issued January 1, 1999, discloses complexes comprising VEGF nucleic acid ligands in association with lipophilic compounds. Floege *et al.*, American Journal of Pathology 154:169-179 (January 1999) discloses complexes comprising PDGF nucleic acid ligands and polyethylene glycol (PEG). Willis *et al.*, Bioconjugate Chemistry 9:573-582 (July 1998) discloses complexes of VEGF nucleic acid ligands and diakylgycerol. See also page 12, lines 13-29 of the specification of the instant application. Thus, this is a mature technology where the level of skill is high and advanced. Furthermore, the level of one of ordinary skill in the art is very high, Ph.d. level or higher. In technologies which are mature, and where the knowledge and level of skill in the art is high, the *Written Description Guidelines* provide (see above) that a written description question should not be raised for original claims even if the specification discloses only a method of making the invention and the function of the invention. In the present case, therefore, even if the specification disclosed only the SELEX method and methods for complexing nucleic acid ligands with non-immunogenic, high molecular compounds or lipophilic compounds, a written description rejection should not be made. The present specification discloses even more than a

method and function, however. The present invention discloses 216 nucleic acid ligands to TGFβ2, and further discloses a specific complex of a TGFβ2 ligand and a polyethylene glycol.

According to the *Written Description Guidelines*, *MPEP* § 2163 II.A.3(a), the "[d]escription of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces." Applicants are in possession of the genus of complexes of TGFβ2 nucleic acid ligands because the SELEX method was well known and advanced, because non-immunogenic high molecular weight compounds and lipohilic compounds were well known, and because methods for attaching such compounds to nucleic acids were well known. Information which is well known in the art need not be described in detail in the specification. See, e.g., *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986).

VIII. CLAIMS APPENDIX

2. A complex comprised of a TGFβ2 nucleic acid ligand and a non-immunogenic, high molecular weight compound or lipophilic compound.

3. The complex of Claim 2 further comprising a Linker between said ligand and said or lipophilic compound.

4. The complex of Claim 2 wherein said non-immunogenic, high molecular weight compound is a polyalkylene glycol.

5. The complex of claim 4 wherein said polyalkylene glycol is polyethylene glycol (PEG).

6. The complex of claim 5 wherein said PEG has a molecular weight of about between 10-80 K.

7. The complex of claim 6 wherein said PEG has a molecular weight of about 20-45 K.

IX. EVIDENCE APPENDIX

Enclosed please find copies of the following references of record in this appeal:

1. WO 96/34876
2. WO 98/18480
3. WO 99/3119
4. U.S. Pat. No. 5,859,228
5. Floege *et al.*, American Journal of Pathology 154:169-179 (January 1999)
6. Willis *et al.*, Bioconjugate Chemistry 9:573-582 (July 1998)

X. CLOSING REMARKS

For the foregoing reasons, Appellant submits that the lack of written description of claims 2-7 has not been established, and that the claims are therefore patentable. Enclosed is a check in the amount of $950.00 to cover the cost of the fee for this Appeal Brief ($500.00) and a two month extension of time ($450.00). It is believed that no other fees are due with this Appeal Brief. If this is in error, please charge any additional fees to Deposit Account No. 19-5117.

Respectfully submitted,

Date: May 31, 2005

Rosemary Kellogg, #39,726
Swanson & Bratschun, L.L.C.
1745 Shea Center Drive, Suite 330
Highlands Ranch, Colorado 80129
Telephone: (303) 268-0066
Facsimile: (303) 268-0065

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